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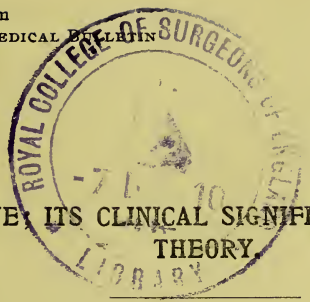

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RED INDICAN URINE; ITS CLINICAL SIGNIFICANCE THE METCHNIKOFF THEORY.

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Five chromogens are met with in the urine—those from the bile and blood, and the three which represent the conjugate or ethereal sulphates. Of the latter, to which have been given the names indican, urohæmatin (indigo-red) and urorosein, respectively, much has been written about the first, and too little about the second and third.

The organic, conjugate, or ethereal sulphates are represented in the daily output of sulphuric acid in the ratio of about 10 for the preformed and 1 for the conjugated, the combined daily output of the preformed and conjugated combinations being between 2 and 3 grammes a day. Taking the substances from which they are derived (indol, skatol and phenol), it may be said that when the production of these in the body is in excess or is beyond the combining power of the oxidase of the hepatic, renal or general tissue cells, they are not firmly bound, and oxidize merely to the indoxyl compounds of potassium, in which forms they are found in the urine. The most thoroughly studied of these is the conjugate potassium indoxyl-sulphate, or indican, which is colorless, but which when treated with strong acids and oxidizing agents is decomposed with the formation of indigo-blue, the color of which is easily recognized. Such urines are seen in cases in which anywhere in the body (as in the contents of the intestines, accumulations of putrid pus, septic peritonitis, empyema, etc.), a decomposition or putrefaction of albuminous substances is taking place. Regarding urohæmatin and urorosein, however, no such definite statement can be made; at least, it can only be stated that these are more complex substances in their make-up than indican alone.

While indican, urohæmatin and urorosein are found in trivial amounts in urine from normal individuals, there is no doubt that when they are present in large amounts they have distinct clinical significance. In entering upon the consideration of those cases in which the origin is intestinal, we find that these bodies have a direct importance in the production of such local conditions as the various forms of chronic enteritis and colitis, in which the mucosa and muscularis are rendered more or less atrophic; in the production of, first, an excess of secretion in the stomach with hypermotility and hypersensibility, and later on a depressing effect on secretion and motility, but not on sensibility (as

I have advanced, I believe that the finding of low or absent gastric secretion in indicanuric cases is a resultant and not the causative condition); to these toxic depressing actions on the correlated functions of the digestive tract are added those on the liver in the under-production of bile and urea and over-production of uric acid, on the pancreas in depressed secretion, and from these, all the effects upon the nutrition of the organism as a whole, and of the nervous system in particular; and, as a last link in the chain, degeneration of certain parenchymatous tissues (nervous, renal, cardiac, hepatic and vascular). In the study of some of my recent cases, I have often been reminded of those instances of homicide described in fiction, in which steady dosing of arsenic, phosphorus or lead eventually brought about a fatal ending. The two groups of cases differ in the nature of the toxic agents, but some of the ethereal sulphate cases show no less certainty in the final harmful results.

From March 1, 1909 to March 1, 1910 I examined 1371 specimens of urine from cases coming under my observation for the first time. Of these, an increased conjugate sulphate partition, represented in the three chromogens, was noted 427 times; 171 showed urorosein alone; 67, indican alone; 166 showed urorosein and indican combined; 20, blue and red indican combined, and 3 urohæmatin alone. As a report of these would prolong the article unduly, each one having a more or less complex clinical make-up, I will limit myself here to the three red indican cases alone, and a mention of some of my views regarding the significance of urorosein. The urinary test which I use is a modification of the Jaffé test, consisting of the addition of an equal part of concentrated hydrochloric acid to the urine (about 5 c.c. of each), then about 2 c.c. of peroxide of hydrogen and about 3 c.c. of chloroform, shaking well, and then centrifuging the whole. This gives the blue and red indican in the chloroform and the urorosein in the supernatant fluid (the red indican and urorosein both being rose-colored).

Urohæmatin is most probably an indoxyl derivative having a clinical significance similar to indican. It is more rarely observed alone than indican, although a purplish color which represents both the blue and the red is a most frequent finding. Red indican urines are often found in extensive disease of the small intestine allowing of resorption, in gastric cancer, and in acute and chronic peritonitis. Like blue indican, it is met with also in ileus and intestinal obstruction, though not so commonly in the malignant and organic strictured states and in chronic diarrhœa. It is present in normal urine in small amounts, and may be demonstrated by shaking the urine with chloroform (about 4 to 1 parts by volume) and decanting it after agitation during several days, when the addition of a drop of concentrated hydrochloric acid to the chloroform will cause the appearance of a rose color—the deeper the color, the greater is the amount of chromogen present. It is probably of albuminoid origin.

Urorosein is probably a derivative of skatol. In the author's modification of the Jaffé test as mentioned above, this chromogen may be extracted from the supernatant fluid by amyl alcohol and separated from other pigments that may be present at the same time by shaking with sodium hydrate, by which the

solution is decolorized. Upon the addition of one or two drops of hydrochloric acid to the alcoholic extract the rose-red color of urorosein reappears, quickly fading out on standing. It is interesting to observe that while both indicans are found in cases of albuminoid putrefaction in the intestines, urorosein is more commonly found where there is fermentation of vegetable substances, as in cases of saccharo-butyric chronic intestinal putrefaction. These cases of putrefaction may have neither blue nor red indican in the urine (only urorosein), and they comprise by far the greatest number of cases of chronic intestinal putrefaction of all forms that exist.

The blue indican cases usually present themselves clinically showing depression, relaxation, lowered vitality and persistent anæmia. The red indican cases, on the other hand, are more usually of the irritative, anxious, highly neurotic and hysterical types, with good general body and blood conditions, and are not so commonly constipated. In this way they are more like the urorosein cases although more pronounced. My experience has been that the bacterial and cultural examinations of the fæces in the blue and red indican cases show no distinctive differences. Some yield high Gram-positive findings, others low. In the urorosein cases, however, the Gram-positive diplococci and bacillus aërogenes capsulatus are almost always high. It must not be forgotten that just as these chromogens differ in findings, amounts and combinations, different bacterial results in the fecal examinations are also met with. After such conditions have existed for a while, improperly or negatively treated, or not under observation, the different bacterial species usually proliferate hand in hand; often one type of a distinctive kind will present phases of difference as time goes on, and it may even develop into another type while the case is under observation. It is almost a daily observation with me that when the proper diet for an indican case has been maintained for a while (essentially proteid free), and the output of indican has been lowered, the individual will develop into a urorosein case for which the diet would be essentially proteid in make-up. Among other things that must be done in the handling of these cases is to put all types on a diet of proper caloric value to meet the weight and work of the individual, and to grade the proteins, protein sparers and vegetables to meet the urinary indications. Only in this way can substantial tissue-construction in treatment take place.

The carrying out of such a treatment is difficult and requires close watching and much labor in the laboratory. For these cases there is no short cut of therapy like the Metchnikoff Bulgarian bacillus milk treatment. The hundreds of patients with these conditions whom I have observed and whose urines and fæces I have exhaustively examined from time to time have definitely proven this to be so, even in the face of the good reports that are being advanced from the use of this milk. The worst cases of indolic putrefaction of the gut I have seen were using this milk for weeks without improvement. Let us not forget that an individual on a diet of good milk harbors less bacteria in the colon than when on any other kind of diet, simply because the constituents of milk are of such kinds and in such forms that they are all quickly digested and absorbed, and leaving but little residue to accumulate in the colon. We long

ago learned empirically that there was some special value in milk diets, and that is why milk has been used these many years in our hospitals as a food for the very ill. It is entirely a matter of how much and what kind of foods pass through the ileocecal valve, past further digestion and absorption, for accumulation in the colon, in which organ these organisms are rife and can attack them. I predict that in ten years from now the fallacy of the inhibitory effects of the Bulgarian bacillus on other organisms in the gut will be so plainly and broadly understood that the use of this milk will be only of historic interest in medicine, and that special dieting and vaccination, with old-fashioned remedies, will then hold general sway in the handling of these cases.